```
 1v MASMTGGQQM GRGSMAGVLP AHGTQHGIRL PLRSGLGGAP LGLRLPRETD
36p EEPEEPGRRG SFVEMVDNLR GKSGQGYYVE MTVGSPPQTL NILVDTGSSN
 38 FAVGAAPHPF LHRYYQRQLS STYRDLRKGV YVPYTQGKWE GELGTDLVSI
 88 PHGPNVTVRA NIAAITESDK FFINGSNWEG ILGLAYAEIA RPDDSLEPFF
138 DSLVKQTHVP NLFSLQLCGA GFPLNQSEVL ASVGGSMIIG GIDHSLYTGS
188 LWYTPIRREW YYEVIIVRVE INGQDLKMDC KEYNYDKSIV DSGTTNLRLP
238 KKVFEAAVKS IKAASSTEKF PDGFWLGEQL VCWQAGTTPW NIFPVISLYL
288 MGEVTNQSFR ITILPQQYLR PVEDVATSQD DCYKFAISQS STGTVMGAVI
                              T2←
338 MEGFYVVFDR ARKRIGFAVS ACHVHDEFRT AAVEGPFVTL DMEDCGYNIP
     T1←
388 QTDESTLMTI AYVMAAICAL FMLPLCLMVC QWRCLRCLRQ QHDDFADDIS

438 LLK*
```

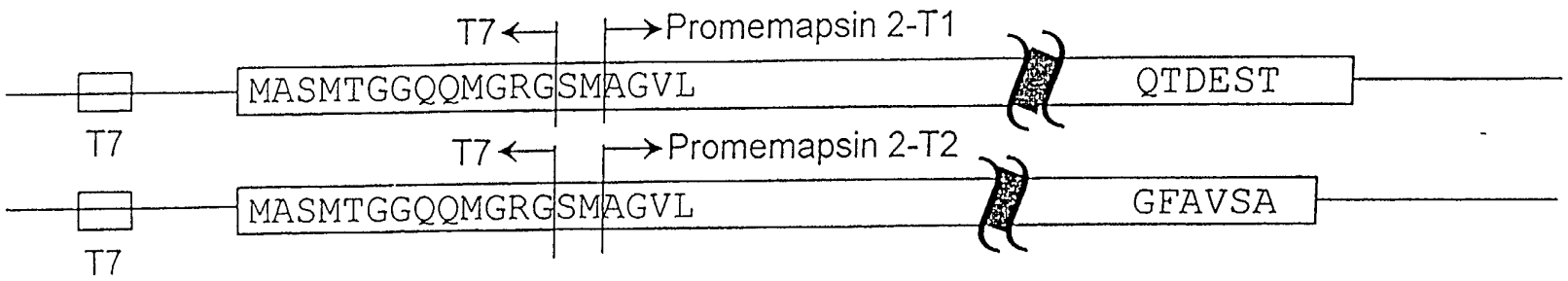


FIG. 1

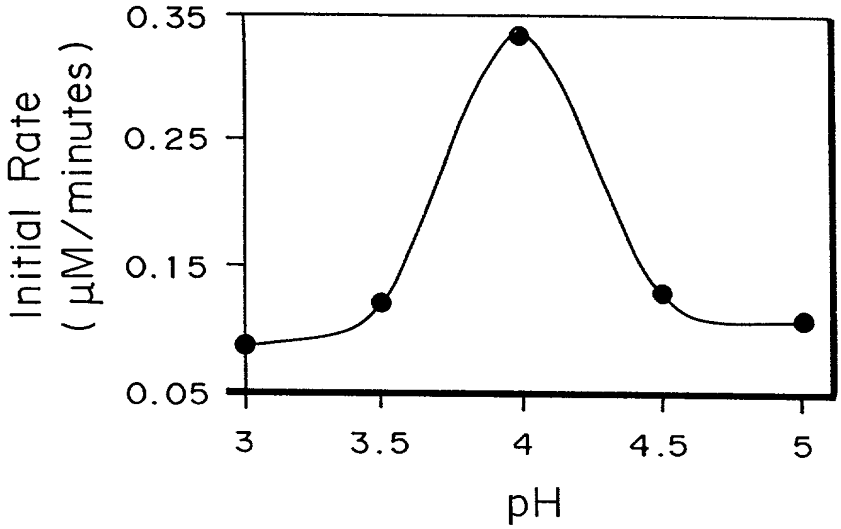

0.35
0.25
0.15
0.05
Initial Rate
(µM/minutes)
3
3.5
4
4.5
5
pH

FIG. 2A

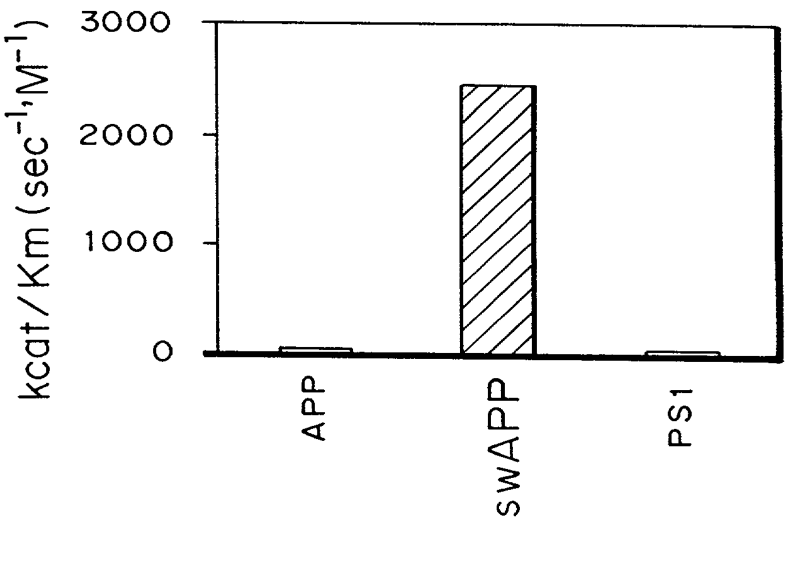

3000
2000
1000
0
kcat/Km(sec⁻¹,M⁻¹)
APP
swAPP
PS1

FIG. 2B

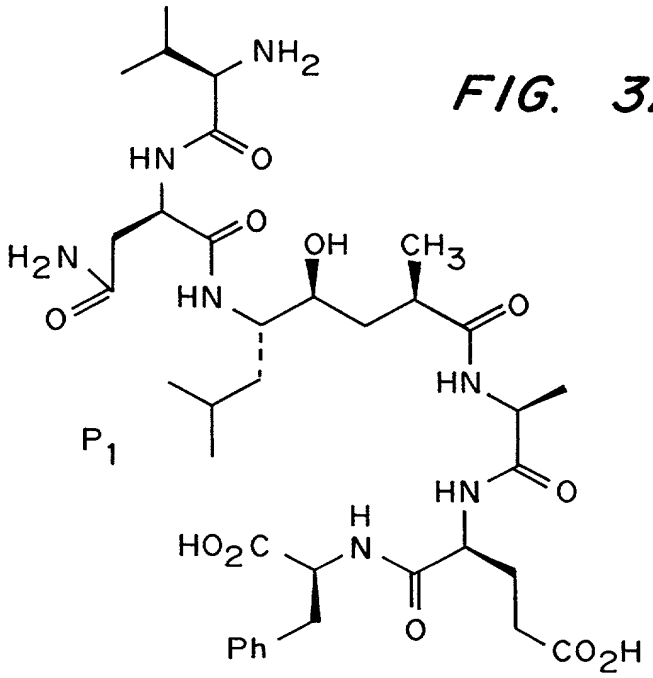


FIG. 3A

OM99-1

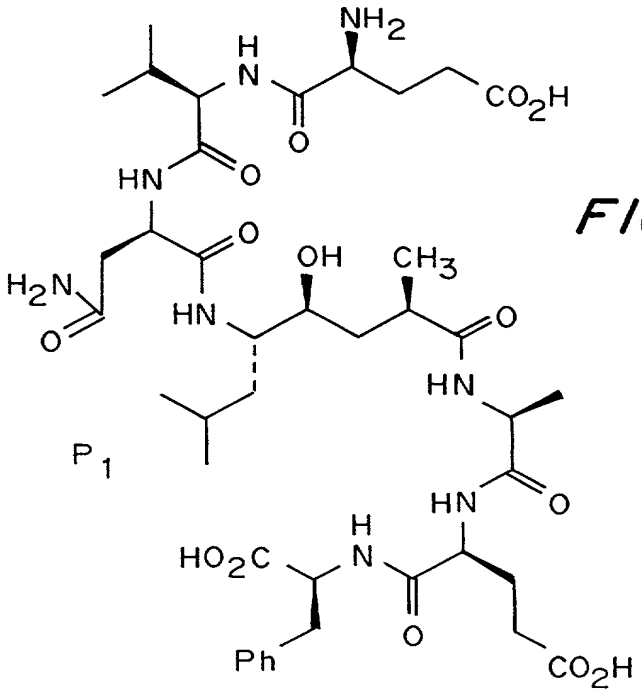
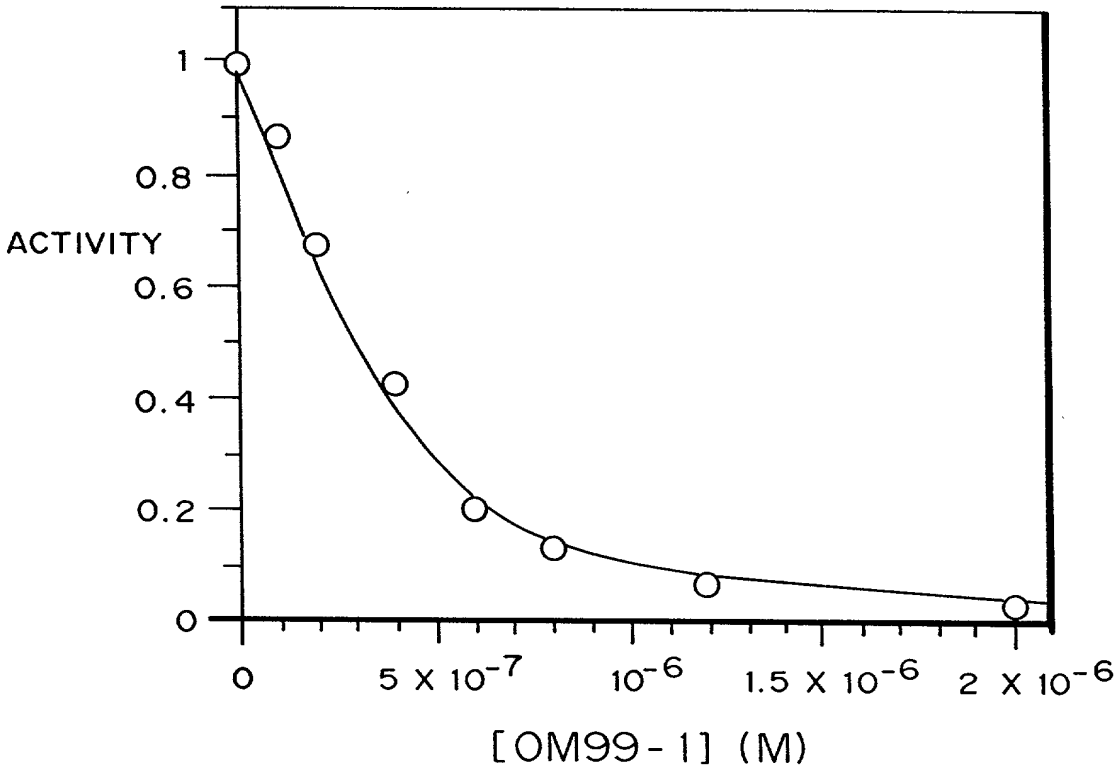


FIG. 3B

OM99-2

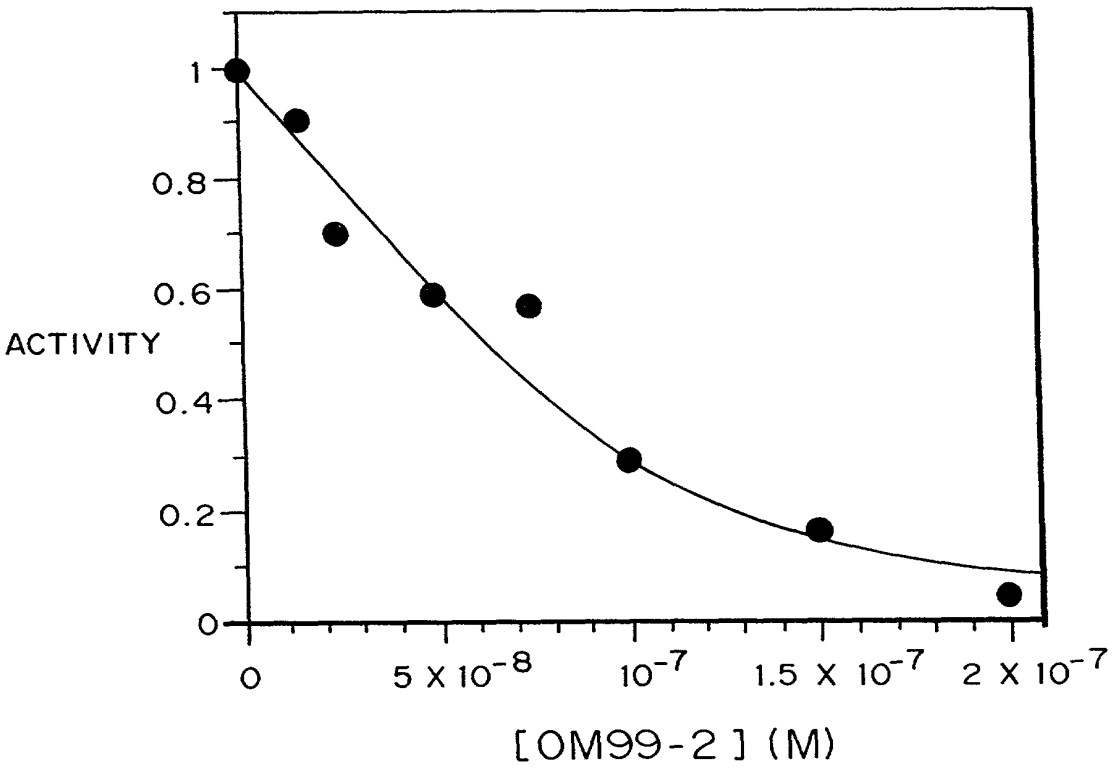
FIG. 4A



[Mep2] = 0.47 μM
[Fluo. Substrate] = 29.9 μM
Buffer: Na Acetate 0.1 M, 5% DMSO, pH 4.5 at 37°C
Excitation at 350 nm
Emission at 490 nm

Parameter	Value	Std. Error
Ki	6.84e-8	2.72e-9

FIG. 4B



[E]o = 0.11 μM
[Fluo Substrate] = 29.9 μM

Parameter	Value	Std. Error
Ki	9.58e-9	2.86e-10

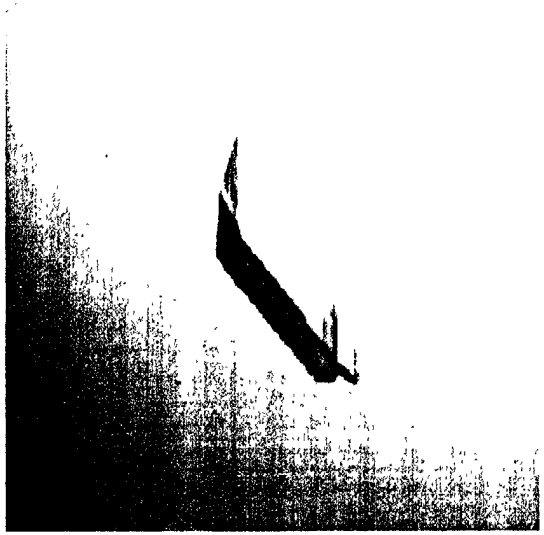


FIG. 5A

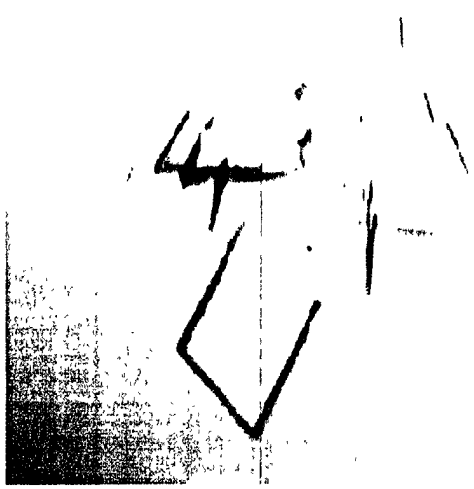


FIG. 5B

FIG. 5C

FIG. 5D

FIG. 5E

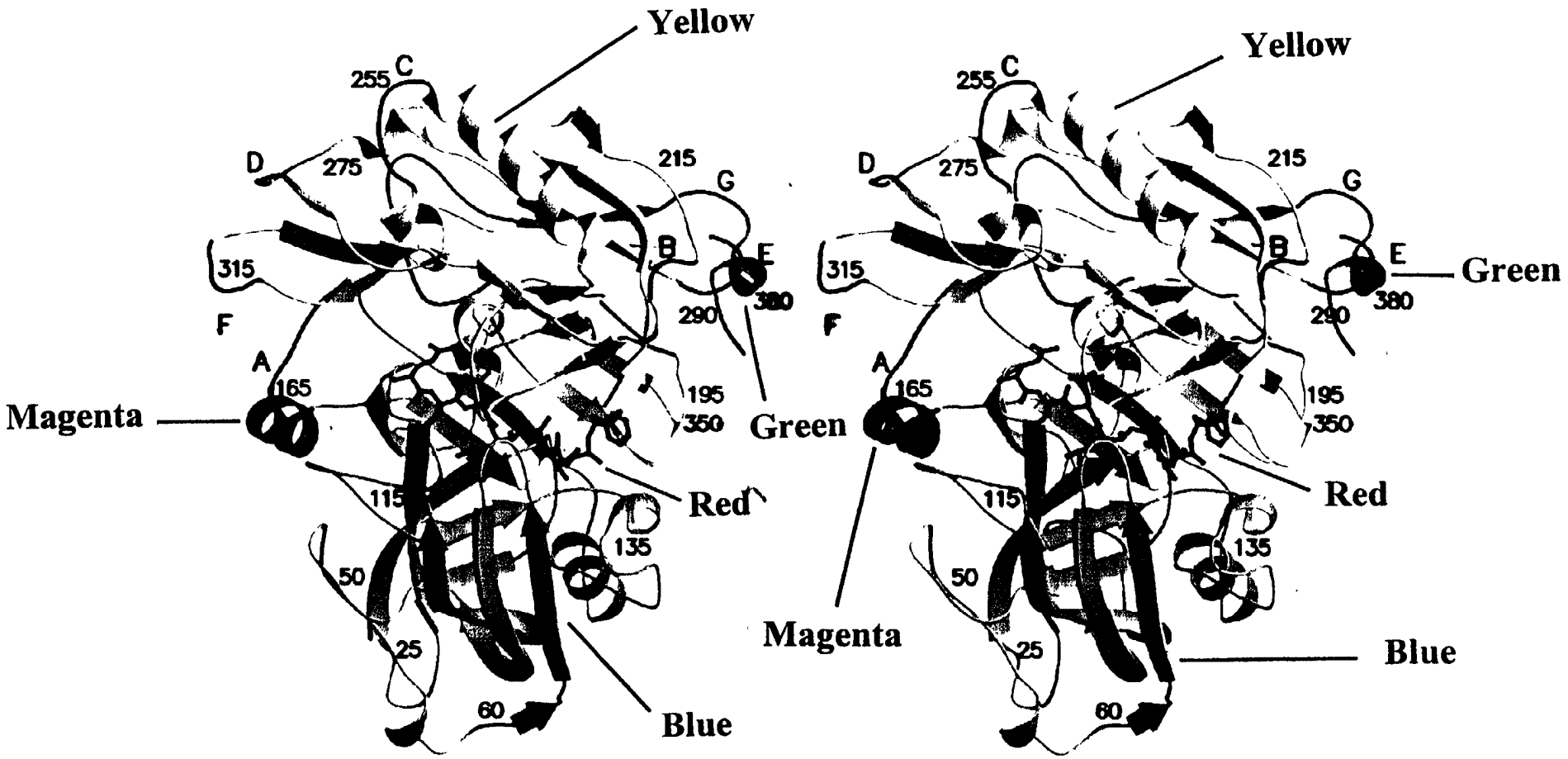


FIG. 6

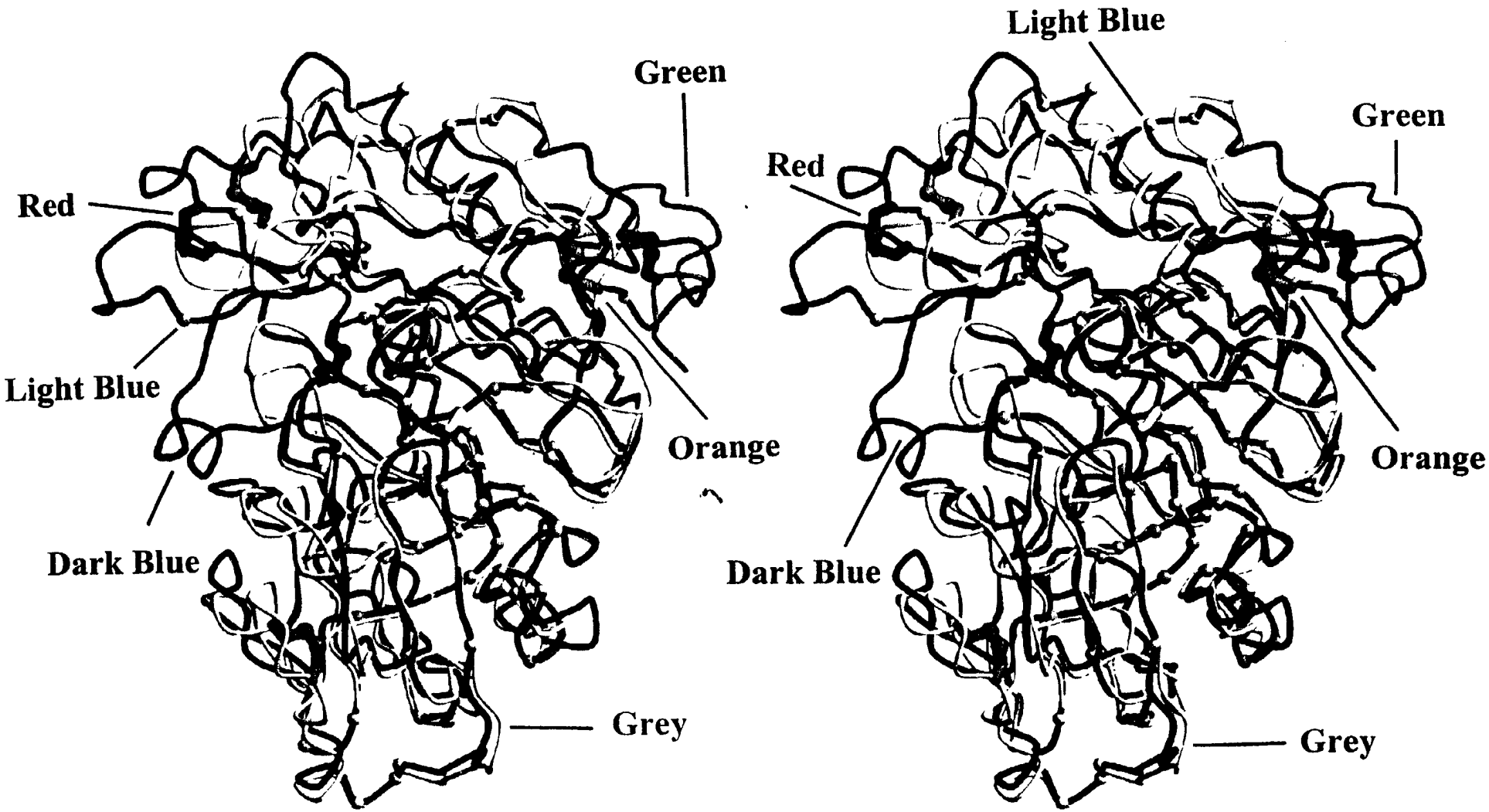


FIG. 7

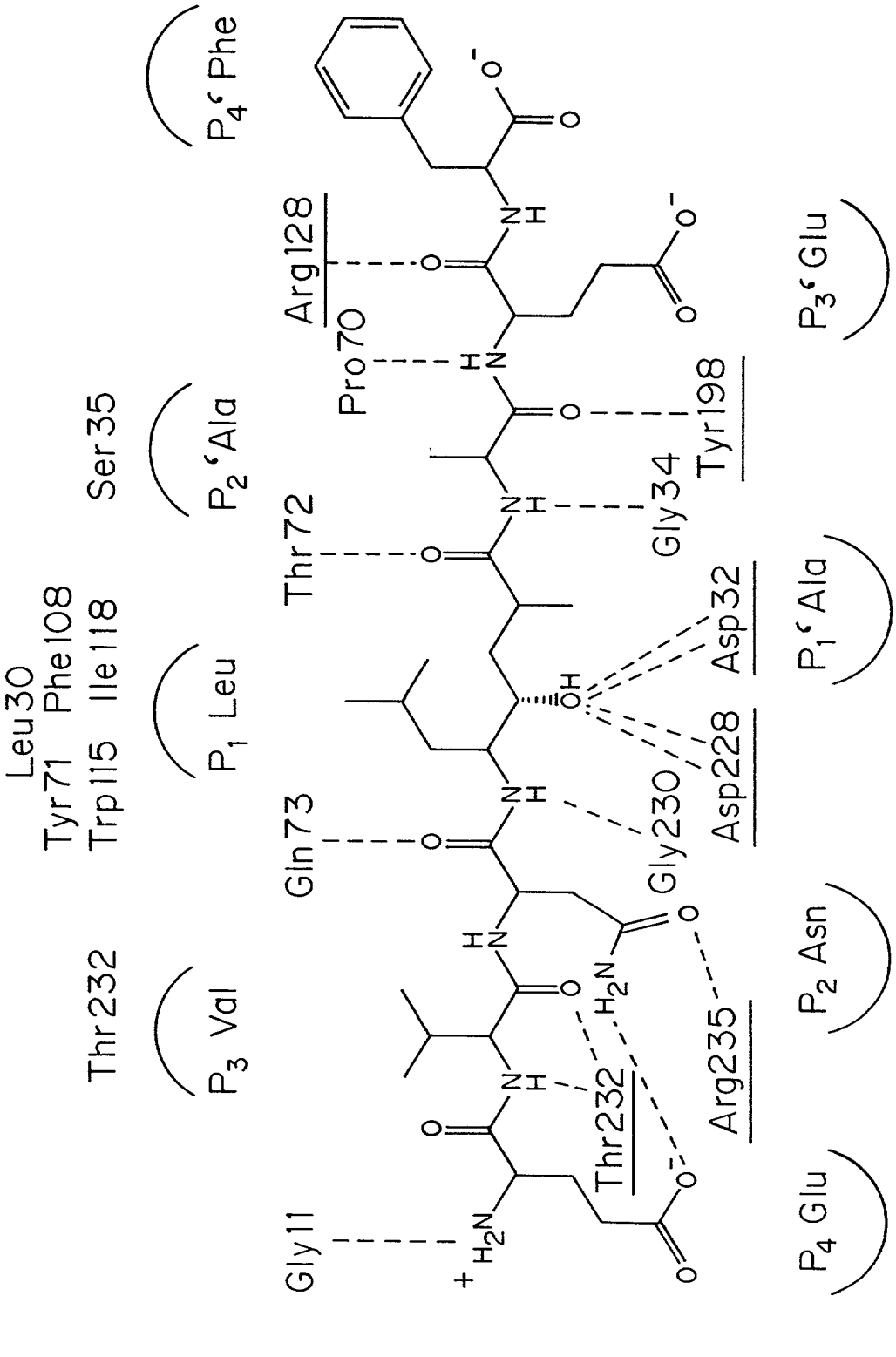

P4' Phe
P2' Ala
P1' Ala
P3' Glu
P3 Val
P1 Leu
P2 Asn
P4 Glu
Arg128
Pro70
Thr72
Gln73
Gly11
Thr232
Leu30
Tyr71
Trp115
Phe108
Ile118
Ser35
Gly34
Tyr198
Asp32
Asp228
Gly230
Arg235
Thr72 Ile226
Asp228
Thr72 Gln73
Thr231 Arg235
Thr232 Asn233
Arg235

FIG. 8

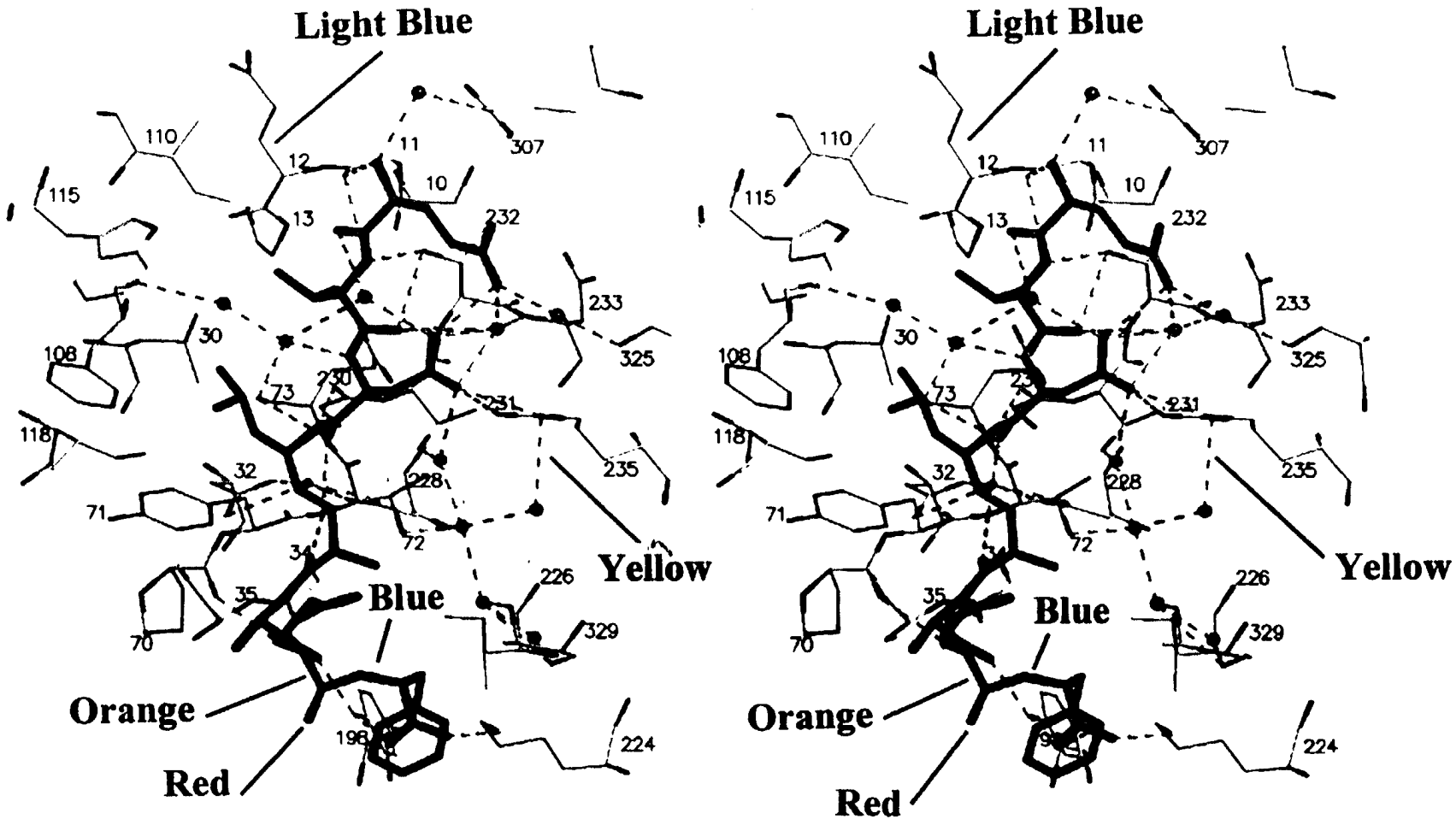


FIG. 9

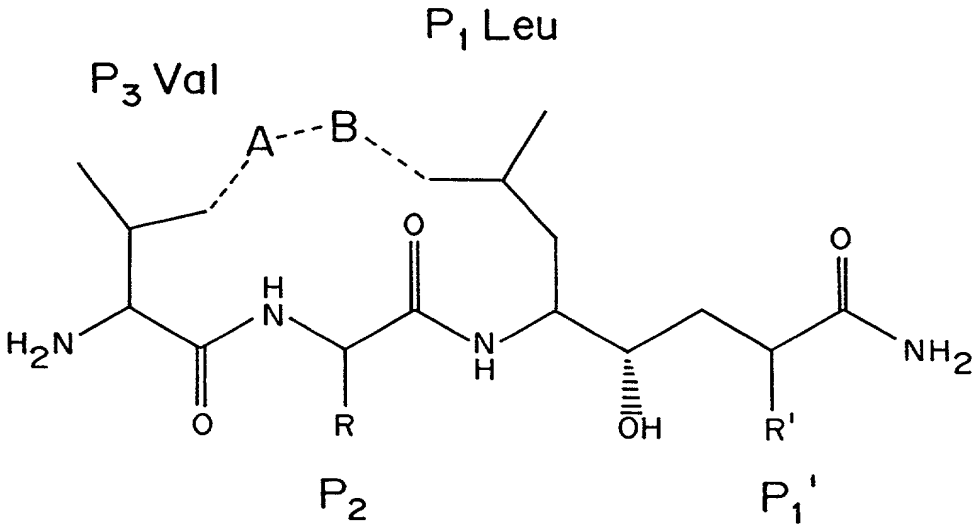


FIG. 10

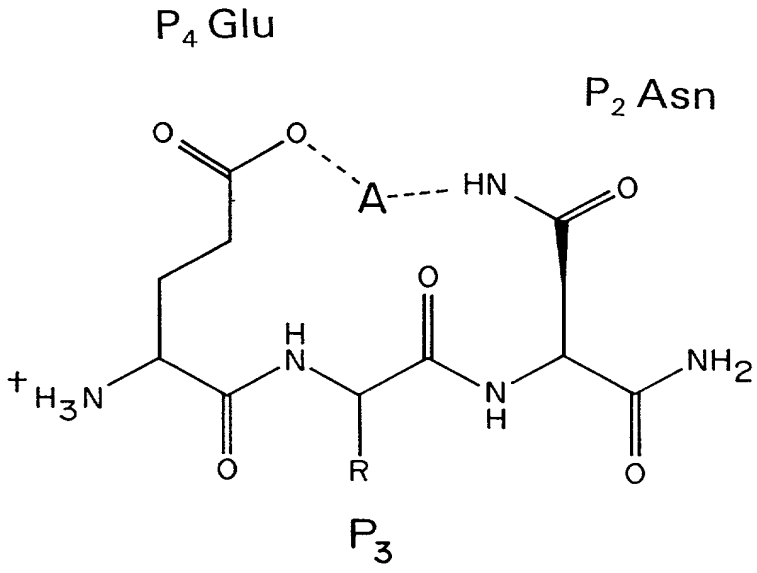


FIG. 11

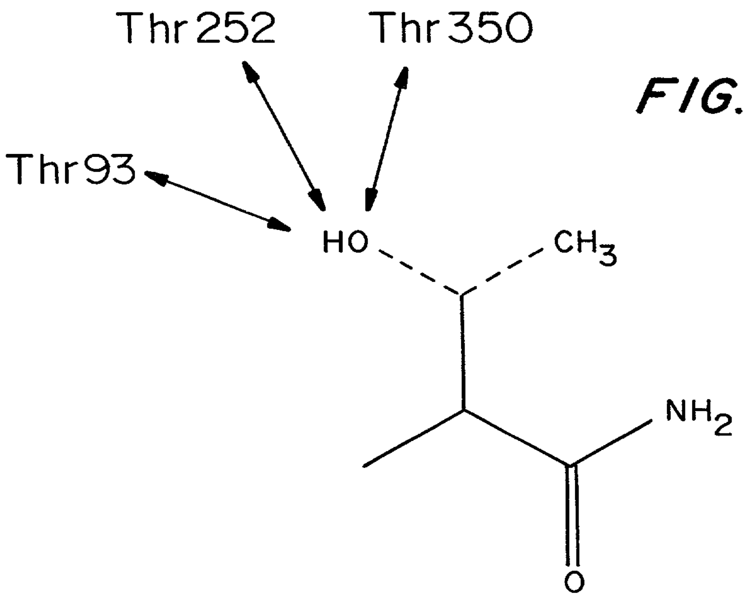

Thr252
Thr350
Thr93
HO
CH3
NH2
O

FIG. 12

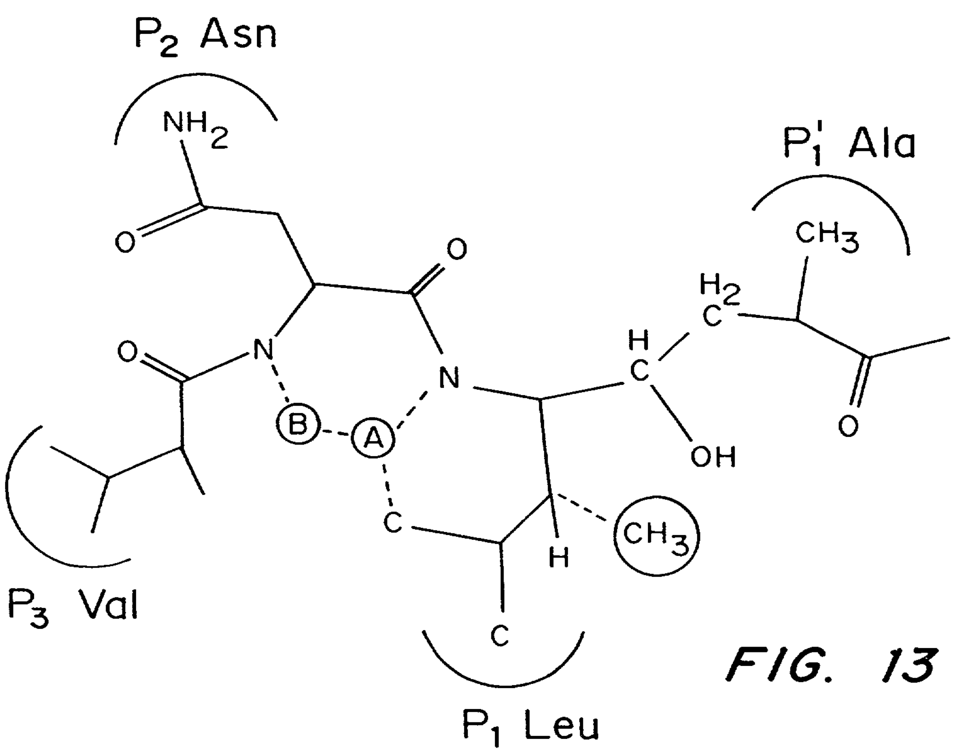

P2 Asn
NH2
O
O
O
N
N
B
A
C
C
H
C
OH
H2
C
CH3
O
CH3
H
P1' Ala
P3 Val
P1 Leu

FIG. 13